

## REMARKS

### **I. Status of the Claims and Restriction**

Claims 1-7 and 11-30 are pending in the application and claims 2, 6, 16-21 and 24-29 stand withdrawn pursuant to the election of species. Thus, claims 1, 3-5, 7, 11-15, 22 23 and 30 are under examination and stand rejected under 35 U.S.C. §103. The specific grounds for rejection, and applicant's response thereto, are set out in detail below.

### **II. Election of Species**

The examiner has indicated that non-elected subject matter must be canceled. Applicants traverse. Since the elected subject matter is properly linked by generic, *i.e.*, "linking" claims, applicants are entitled rejoinder following determination of otherwise allowable subject matter. Thus, to amend the claims now to recite the particular species elected is deemed unduly burdensome.

### **III. Rejections Under 35 U.S.C. §103**

Claims 1, 3-5, 10-15, 22, 23 and 30 stand rejected as obvious over Jappelli in view of U.S. Patent 6,365,347 and Dostmann *et al.* According to the examiner, Jappelli teaches an assay similar to the claims of the present application, using a two-hybrid-like system to screen a peptide library for molecules with binding activity, but where the target for those peptides was an intact protein. The secondary references are cited for the use of peptides smaller than those of Jappelli, but these similarly teach peptide-protein interaction, not peptide-peptide interactions. Applicants traverse.

Applicants note that the examiner's comparison of the instant claims and Jappelli equates the LEP with a 347-residue protein. This is improper. The LEP of the present invention is not the target, it is the *binding partner*. However, in order to highlight some of the differences in the instant invention, applicants have amended the claims to introduce the recitation of claim 10, which states that the LEP is 5-50 residues in length, into claim 1. Thus, given that Jappelli fails to teach or suggest a peptide-peptide assay, this reference alone cannot support the rejection. Similarly, the secondary references also fail in this regard. First, the '347 patent merely provides *one* peptide of 4-16 amino acids, and Dostmann similarly provides *one* peptide of 8-14 residues. Neither reference teaches a peptide-peptide interaction (*i.e.*, between *two* peptides). Thus, taken together, the cited references fail to establish a *prima facie* case of obviousness.

This same argument was advanced in the prior response, although stated in somewhat different terms, *i.e.*, a linear-*versus*-folded argument. The examiner argued that such was irrelevant since Jappelli does not distinguish between linear and folded epitopes. The point, however, was that Jappelli exemplified a complex 347-residue target protein capable of forming folded epitopes, and thus could not possibly predict the interaction of an 8-15 residue target peptide with a 5-50 residue LEP as set forth in the present invention. This aspect of the present application constitutes a far more difficult and unpredictable goal: binding of two small molecules (a target peptide and a LEP), one of which represents a discrete region. Moreover, the target peptide-LEP interaction faithfully represented the binding capabilities of the corresponding region from the target protein. In other words, the specific target sequence was taken out of the context of the target protein and used in a much more convenient *peptide* form. These peptides were screened against LEPs and were able to identify agents that can bind to the intact protein. This feature of the present invention is completely absent from the cited art.

To highlight the nonobvious nature of the invention, applicants are attaching a declaration under 37 C.F.R. §1.132 from Dr. Brent Iverson. In his declaration, Dr. Iverson states that it was indeed unpredictable that *two* peptides could interact in the claimed assay. This was for at least two distinct reasons – lack of conformational stability, and lack of molecular contact points – as compared to a polypeptide-peptide interaction. In light of this evidence, applicants submit that the requisite predictability is missing from the examiner's alleged *prima facie* case.

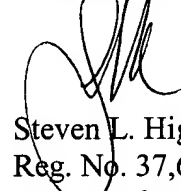
Turning to the remaining two rejections, which rely on the additional teachings of U.S. Patents 6,214,561, and 6,610,495, these references fail to correct the defects described above. Rather, these references are cited for particular features of the assays, and they do not present any teachings that would suggest that one could or should employ a binding assay screen involving not one but *two* peptides, much less that there would be a reasonable expectation of success in so doing. As such, these rejections should fall as well.

In summary, Jappelli *et al.* is only relevant to the present invention on the grounds that the screening technique used was similar to that employed by the inventor here. But unlike Jappelli, or any of the secondary references, the present invention utilizes two peptide binding partners in assays for identifying binding regions of larger target molecules. Not only had this not been done previously, there was widespread doubt as to whether such could be achieved prior to the work of the inventor. Reconsideration and withdrawal of the rejection is therefore respectfully requested.

#### IV. Conclusion

In light of the foregoing, applicant respectfully submits that all claims are in condition for allowance, and an early notification to that effect. Should the examiner have any questions regarding this response, a telephone call to the undersigned is invited.

Respectfully submitted,



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